

## RE: Effects of *Helicobacter pylori* Treatment on Gastric Cancer Incidence and Mortality in Subgroups

We read with interest the recent follow-up of the Shangdong Intervention Trial (1). In that study, volunteers received what is now recognized as a regimen with low eradication success and have been followed for more than 15 years without additional treatment. A reduction in cancer risk was confirmed over time. During the interval, the study has been in progress and it has become clear that *Helicobacter pylori* infection is responsible for the vast majority of gastric cancer and that cancer can be prevented if *H. pylori* eradication is accomplished before atrophic damage occurs (2). *H. pylori* eradication at later times also has a benefit in that it stops the progression of damage and the age-related increase in cancer incidence. Even in those at the highest risk (ie, those who have experienced an early gastric cancer), *H. pylori* eradication reduces the risk of metachronous cancer (3,4). A number of studies have shown that *H. pylori*-host cell interactions can in themselves cause genetic instability, including double-stranded DNA breakage, providing an additional rationale for *H. pylori* eradication (2,5). In 2013, the Japanese government instituted a program of *H. pylori* eradication and surveillance to eliminate gastric cancer from that country (6). Nowhere can we find a statement that

all the participants in the study have been or are being offered effective anti-*H. pylori* therapy and confirmation of cure. Effective regimens have been identified in China, and this is now easily accomplished (7). US government-sponsored research carries the legacy of the Tuskegee and the Guatemala syphilis experiments. Continued failure to end this experiment by providing *H. pylori* eradication, in our opinion, can not be justified and is long overdue.

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### References

1. Li WQ, Ma JL, Zhang L, et al. Effects of *Helicobacter pylori* treatment on gastric cancer incidence and mortality in subgroups. *J Natl Cancer Inst*. 2014;106(7):dju0116 doi:10.1093/jnci/dju116.
2. Shiotani A, Cen P, Graham DY. Eradication of gastric cancer is now both possible and practical. *Semin Cancer Biol*. 2013(6 Pt B):492–501.
3. Fukase K, Kato M, Kikuchi S, et al. Effect of eradication of *Helicobacter pylori* on incidence of metachronous gastric carcinoma after endoscopic resection of early gastric cancer: an open-label, randomised controlled trial. *Lancet*. 2008;372(9636):392–397.
4. Yoon SB, Park JM, Lim CH, et al. Effect of *Helicobacter pylori* eradication on metachronous gastric cancer after endoscopic resection of gastric tumors: A meta-analysis. *Helicobacter*. 2014;19(4):243–248.
5. Hanada K, Graham DY. Helicobacter pylori and the molecular pathogenesis of intestinal-type gastric carcinoma. *Expert Rev Anticancer Ther*. 2014;14(8):447–454.
6. Asaka M. A new approach for elimination of gastric cancer deaths in Japan. *Int J Cancer*. 2013;132(6):1272–1276.
7. Liang X, Xu X, Zheng Q, et al. Efficacy of bismuth-containing quadruple therapies for clarithromycin-, metronidazole-, and fluoroquinolone-resistant *Helicobacter pylori* infections in a prospective study. *Clin Gastroenterol Hepatol*. 2013;11(7):802–807.

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### Notes

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